

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | | |
|--|---|---|------------------|
| Applicant's or agent's file reference 30928P WO | FOR FURTHER ACTION | | See item 4 below |
| International application No. PCT/EP2004/006916 | International filing date (<i>day/month/year</i>) 25 June 2004 (25.06.2004) | Priority date (<i>day/month/year</i>) 26 June 2003 (26.06.2003) | |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | | |
| Applicant MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN E.V. | | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

| | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

Date of issuance of this report
03 January 2006 (03.01.2006)

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| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35 | Authorized officer Ellen Moyse Telephone No. +41 22 338 89 75 |
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PATENT COOPERATION TREATY

REC'D 26 NOV 2004

From the
INTERNATIONAL SEARCHING AUTHORITY

WIPO PCT

To:

see form PCT/ISA/220

6/1

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

| | | |
|---|--|---|
| | | Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet) |
| Applicant's or agent's file reference see form PCT/ISA/220 | | FOR FURTHER ACTION See paragraph 2 below |
| International application No. PCT/EP2004/006916 | International filing date (day/month/year) 25.06.2004 | Priority date (day/month/year) 26.06.2003 |
| International Patent Classification (IPC) or both national classification and IPC G01N21/64, C07D221/04, C09B23/12 | | |
| Applicant MAX-PLANCK-GESELLSCHAFT ZUR FOERDERUNG DER ... | | |

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d

Authorized Officer

Michalitsch, R



WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/006916

Box No. 1 Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/006916

Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|-------------|
| Novelty (N) | Yes: Claims | 2,9 |
| | No: Claims | 1,3-8,10,11 |
| Inventive step (IS) | Yes: Claims | 9 |
| | No: Claims | 1-8, 10-11 |
| Industrial applicability (IA) | Yes: Claims | 1-11 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item V.

1. The following documents are referred to in this communication:

D1 : ZECK G. ET AL: "Noninvasive neuroelectronic interfacing with synaptically connected snail neurons immobilized on a semiconductor chip" PROC. NATL. ACAD. SCI., vol. 98, no. 18, 28 August 2001 (2001-08-28), pages 10457-10462.

D2: KUHN BERND ET AL: "Anellated hemicyanine dyes in a neuron membrane: Molecular Stark effect and optical voltage recording" J PHYS CHEM B; JOURNAL OF PHYSICAL CHEMISTRY B AUG 7 2003, vol. 107, no. 31, 7 August 2003 (2003-08-07), pages 7903-7913.

2. Novelty (Art. 33(2) PCT) and Inventive Step (Art. 33(3) PCT).

2.1. INDEPENDENT CLAIM 1

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

Document D1 discloses a method of determining voltage changes by means of a voltage sensitive dye (D1, p.10458, right column, ANNINE-5), wherein the fluorescence of the dye is measured.

According to D1, the excitation of the dye is carried out at 472 nm, which appears to correspond to an absorption around 20% relative to the maximum absorption wavelength for ANNINE 5 (as estimated by the data in D2). Consequently this feature appears to be included in the teaching of D1 and **Claim 1 of the present application would lack novelty in the sense of Art. 33(2) PCT.**

Even if novelty could be assessed for claim 1, the features of the claim would not provide for an underlying inventive step (Art. 33(3) PCT), since the 20% absorption factor is merely optional and represents a arbitrarily chosen threshold.

2.2. These arguments also apply with respect to claim 2, which lacks an inventive step

(Art. 33(3) PCT) for the same reasons, and moreover is unclear within the meaning of (Art. 6 PCT) due to the multiple definitions of the absorption limits.

- 2.3. The dependent claims 3-8 do not appear to introduce any inventive subject matter, since the features they introduce are known from D1. In particular, the dye structure and materials (claims 7 and 8) are known. Therefore, claims 3-8 do not appear to fulfil the requirements of Art. 33(2) PCT.
- 2.4. The same arguments also apply with respect to claims 10 and 11, which also lack novelty (Art. 33(2) PCT).

3. Inventive Subject matter.

In contrast, claims 7 and 9 in combination with the features introduced in claim 2 do appear to contain novel and inventive subject matter.

The excitation at the very band edge of the absorption spectrum (<2% absorption) in combination with a measurement of the Stark Effect enables a surprising increase in the sensitivity of the voltage determination.
